

# Relevance of Quantum Mechanics in Circuit Implementation of Ion channels in Brain Dynamics

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## Abstract

With an increasing amount of experimental evidence pouring in from neurobiological investigations, it is quite appropriate to study viable reductionist models which may explain some of the features of brain activities. It is now quite well known that the Hodgkin-Huxley (HH) Model has been quite successful in explaining the neural phenomena. The idea of circuit equivalents and the membrane voltages corresponding to neurons have been remarkable which is essentially a classical result. In view of some recent results which show that quantum mechanics may be important at suitable length scales inside the brain, the question which becomes quite important is to find out a proper quantum analogue of the HH scheme which will reduce to the well known HH model in a suitable limit. From the ideas of neuro-manifold and the relevance of quantum mechanics at some length scales in the ion channels, we investigate this situation in this paper by taking into consideration the Schrödinger equation in an arbitrary manifold with a metric, which is in some sense a special case of the heat kernel equation. The next important approach we have taken in order to bring about it's relevance in brain studies and to make connection with HH models is to find out a plausible circuit equivalents of it. What we do realize is that for a proper quantum mechanical description and it's circuit implementation of the same we need to incorporate the non commutativity inside the circuit model. It has been realized here that the metric is a dynamical entity governing space time and for considering equivalent circuits it plays a very distinct role. We have used the methods of stochastic quantization and have constructed a specific case here and see that HH model inductances gets renormalized in the quantum limit.

**Keywords :** Hodgkin-Huxely model, Quantum Mechanics, Circuit Implementation, Ion Channel **PACS No.:**87.10.+e

# 1 Introduction

Nervous systems use electrical signals which propagate through ion channels which are specialized proteins and provide a selective conduction pathway, through which appropriate ions are escorted to the cell's outer membrane. Also, the ion channels undergo fast conformational changes in response to metabolic activities which opens or closes the channels as gates. The gating is essentially changes in voltages across the membrane and ligands. The voltage dependent ion channels have an ability to alter ion permeability of membranes in response to changes in transmembrane potentials. The magnitude of current across membrane depends on the density of channels, conductance of the open channel and how often the channel spends in the open position or the probability. Hodgkin and Huxley [1, 2] accounted for the voltage sensitivity of  $\text{Na}^+$  and  $\text{K}^+$  conductance of the squid giant axon by postulating charge movement between kinetically distinct states of hypothetical activating particles. In spite of the detail electrophysiological studies, the atomic structure of voltage gated ion channels still remained in the dark till the discovery of Mckinnon and his collaborators [3, 4, 5] which obtained a crystal structure of a  $\text{Ca}^{2+}$  gated  $\text{K}^+$  ion channel provides a mechanism for gating [6, 7]. A functional study of *KvAP* in this context led to a proposal known as the voltage sensor paddle model.

Considering the voltage sensor capabilities of the ion channels and generation of currents and potentials, we in this paper deal mainly with the electrical properties of the ion channels. It is already known that the neuron acts as an electrical device, [8] where a potential difference develops across the membrane due to differences in ion concentrations between inside and outside the cell. The participating ions are Sodium( $\text{Na}^+$ ), Potassium ( $\text{K}^+$ ), Calcium ( $\text{Ca}^+$ ) and Chlorine( $\text{Cl}^+$ ). Nernst equation describes equilibrium potential for a single ionic species as

$$E = \frac{RT}{zF} \ln \frac{[X^+]_o}{[X^+]_i}$$

Membrane potential due to the combined permeability of different ionic species is given by the Goldman-Hodgkin-Katz equation

$$V_m = \frac{RT}{zF} \ln \frac{K_o + [p_{\text{Na}}/p_{\text{K}}]\text{Na}_o + [p_{\text{Cl}}/p_{\text{K}}]\text{Cl}_i}{K_i + [p_{\text{Na}}/p_{\text{K}}]\text{Na}_i + [p_{\text{Cl}}/p_{\text{K}}]\text{Cl}_o} \quad (1)$$

Total membrane current is given by the sum of individual channel currents

$$I_m = I_{\text{Na}} + I_{\text{K}} + I_{\text{Cl}}$$

In this way, a membrane patch can be described by an equivalent electrical circuit component. As we have discussed earlier, electrical signals are changes in the membrane potential at specific sites of the neuronal network, which are obtained by changes due the closing and opening of ion channels. Given these things to be known, the main objective of this paper is different. In a recent article [9] it has been hypothesized by some dimensional

arguments that quantum mechanics may be operative at some scale in the ion channels. If this is the case then the whole story of voltage sensing in ion channel gets a new paradigm shift. If we assume that membrane voltage and currents are generated through equivalent circuits but at length scales where quantum mechanics is assumed to hold, then due to noncommutative effects the whole concept of devising electrical circuits is different, but also at the same time it should be mentioned here that at large length scales corresponding to a large collection of ion channels in comparison to a single or few ion channels in the previous case, we expect the quantum effects to average out and the conventional circuit elements for describing the mechanisms of voltage [10] and current generation through the gates is valid.

In this paper, we implement a quantum circuit for the ion channels following the lines of [11]. The basic task in hand is as follows, we have developed a Schrodinger equation and a implementation of the equivalent circuit. Now following the work [12] on neuromanifolds we assume that the underlying geometry of the ion channels is not known a priori. Thereby we assume a curved manifold and write down the nonlinear Schrödinger equation (NLSE), essentially a heat kernel equation in a curved manifold [13]. The next task in hand is to find out an equivalent circuit model for that. In the last section we find out a connection with the HH model and determine how the quantum effects may get lost at large length scales in the mesoscopic case when we take the limiting case of large number of ion channels.

## 2 Hodgkin-Huxley Equations

The model we would like to describe is a neuronal model at length scales of ion channels where we believe that quantum mechanics may be operative. But we believe that the model may also include the HH model as a special case where coarse graining can be done, or for example, if we include large number of channels, the collective behaviour should be described by the HH model. For the sake of completeness, we would like to describe the HH model in brief [14].

In the HH case, the basic membrane circuit suitable for, say, a squid giant axon with two voltage dependent channels is given by the following construction: The circuit is described by a capacitor  $C$ , sodium, potassium, leakage conductance  $G_{Na}$ ,  $G_K$  and  $G_L$  respectively. The membrane potential is the voltage difference between the outside and inside of the cell membrane and there can be a current injected into the cell from an electrode or other parts of the cell.

The equations describing the phenomena is given by

$$C \frac{dV}{dt} = I_{ext} - G_{Na}(V - E_{Na}) - G_K(V - E_K) - G_L(V - E_L) \quad (2)$$

$G_{Na}$  and  $G_K$  are the functions of membrane potentials and time and are given by the

following equations,

$$G_{Na} = \overline{G_{Na}} m^3 h \quad \frac{dm}{dt} = \frac{m_\infty(V) - m}{\tau_m(V)} \quad \frac{dh}{dt} = \frac{h_\infty(V) - h}{\tau_h(V)} \quad (3)$$

$$G_K = \overline{G_K} n^4 \quad \frac{dn}{dt} = \frac{n_\infty(V) - n}{\tau_n(V)} \quad (4)$$

Here  $m^3 h, n^4$  can be interpreted as the opening probability of a channel. The  $Na$  channel has two set of gates i.e., activation gates represented by  $m$  and inactivation gates represented by  $h$ . The activation gates open and the inactivation gates close when the membrane depolarizes. The  $K$  channel has only single activation variable which is a 4 parameter system.

So we see that the state vector variables of the HH model are  $V, m, h, n$ . The equations [2,3] and [4] can be written in a compact matrix notation as

$$\dot{\vec{X}} = \vec{F}(\vec{X}) \quad (5)$$

where  $\vec{X} = [V, m, h, n]^T$ . Equation [5] is a nonlinear equation and mainly numerical methods are employed in solving such equations. We will not go into details of those analysis as here we are interested to carry out the analysis in terms of the relevance of quantum mechanics in ion channels and develop a framework for that and then to see if there exist any limit for which it will reduce to the HH model. More interestingly, the observation that understanding ion channel dynamics is stochastic in nature has prompted us to look at the relevance or analog of stochasticity in the quantum case. A similarity of the HH model with the cellular automation has been observed, [15, 16, 17] which in the limit of large ion channel density gives rise to a Langevin description. Using the Stratonovich description, the HH model is rewritten in the Langevin form as

$$\frac{d}{dt} x_i = A_i(x) + B_{ij} \eta_j(t) \quad (6)$$

where  $i, j = 1 \cdots n$  for the  $n$  channels and  $A_i, B_{ij}$  are related with the moments of the underlying transition probability.

It is striking that HH formulation yields into a noisy model in the large ion channel number limit. This observation has become very crucial in our proposal of the general formulation of the HH formalism in the quantum case.

### 3 Nonlinear Shrödinger Equation (NLSE) and the relation of Stochastic geometry with Neural Modeling

Very Recently the NLSE has been solved with an artificial neural network scheme. This analysis gives us an insight and confidence that maybe the NLSE will play an important

role in analyzing realistic neuronal modeling. Here we discuss in brief about the solution of NLSE on a network for the sake of the completeness of our proposed argument.

The time dependent propagation of light pulse inside a single mode nonlinear optical fiber is given by the solution of

$$i(\frac{\partial \Psi}{\partial z}) - \alpha(\frac{\partial^2 \Psi}{\partial z^2}) - \beta \|\Psi\|^2 \Psi = 0 \quad (7)$$

where  $\Psi$  is the field amplitude,  $z$  and  $t$  are the optical and time axis respectively,  $\alpha, \beta$  are the dispersive and waveguide coefficients respectively. The competition between pulse dispersion and focussing gives rise to the formation of solitons for a particular input. With suitable boundary conditions a stable soliton is obtained. It has been observed that the solution consists of a 3 layer architecture with 42 hidden nodes [18]. Now to speak of the implications of this result it has been also observed that the knowledge of the upper bound on the field amplitude provides a stopping criterion on the training of the neural network (NN).

It may be pertinent to ask at this stage that what use is of the above scheme to our proposed model. What we believe is that applicability of NLSE on NN gives us a clue that may be the Schrödinger equation is applicable at some length scales in neuronal architecture with an unknown, a priori geometry and the basic objective is to find out the appropriate dynamics for that.

We have already emphasized that the neuronal architecture has a form of geometry with some probabilistic structure on it giving rise to a probabilistic manifold [19]. So the main point of the analysis depends on the identification of a stochastic interpretation to quantum mechanics. The essential ingredient is following. We claim that the operator  $A = b_\nu(x)\partial_\nu + (\frac{\hbar}{2\pi i})\nabla$  is the infinitesimal generator of the stochastic process defined by the Langevin equation

$$dx_\mu(t) = b_\mu(x, t)dt + dW_\mu(t) \quad (8)$$

The importance of this identification is that classical probability theory gets related with quantum mechanics. Now, the next question what we can ask is that we are trying to define the SE in a curved probabilistic manifold. So, apart from a stochastic approach to quantum mechanics, we need something more, i.e., to randomize the metric. Let us assume a Lagrangian, given by

$$L = \frac{m}{2}g_{\mu\nu}(x)\dot{x}_\mu\dot{x}_\nu - V(x) \quad (9)$$

Variation of this Lagrangian gives us the equation of motion in the form of geodesics. If we vary the trajectories and define a stochastic process in terms of the variations with gaussian spread and compare this distribution with the Feynman path integral, we end up with the Riccati equation which is the stochastic analogue of the Schrödinger equation on a curved manifold.

$$\frac{\hbar}{2}\nabla_\mu x^\mu + \frac{m}{2}x^\mu x_\mu = V + \frac{\hbar^2 R}{6m} \quad (10)$$

So we see that stochasticity [20] involves a generation of an effective potential of motion. We will see now that how this may be handled in analyzing the quantum circuits.

## 4 Circuit Implementation Of Schrödinger Equation

It is indeed true that in understanding neural mechanisms, we need nonlinear and dissipative analysis. Now as has been argued in [21] over the years and until recently, if we think of the relevance of quantum mechanics for neuronal dynamics at suitable length scales we should try our hands on quantum dissipative systems. Quantum mechanical systems are inherently open systems. In an open system ,for example, in an atom in a cavity, a process such as spontaneous emission is sometimes viewed as dissipative but if the number of modes is reduced, the process becomes reversible. In comparison, the resistance to electric current flow is reversible, which is typical of closed system. But if we think of quantum circuits the situation is drastically different.

In this context, we cite an particular example: A current driven RC circuit which is identical to a free particle driven by an external force. In absence of the resistor, the system is well described by the charge operator  $Q$  and operator  $\phi$  which satisfy  $[\phi, Q] = i\hbar$ . We would like to mention here that a circuit theory [23, 24] that can describe quantum transport, is particularly important and has potential applications in nanotechnology, molecular devices and beam epitaxy etc [25].

As we have already seen that the electric charges of ions are in fact responsible for the membrane potential and action potential. Generation of the potential therefore gives rise to the possibility of modeling the ion channels through electric circuits, which generate the required potentials. The scheme is devised through a quantum analogue of the corresponding electrical circuit. So our objective is pretty clear. Some very recent results at ionic scales regarding the relevance of Quantum Mechanics (QM) [26], we try to build some viable neuronal models and corresponding electric circuits [27]. But as QM governs the dominant dynamics we have to develop quantum circuits.

In this context, we would like to mention very important work [11] which we earlier mentioned, related to the circuit equivalent of Schrodinger's equation. The circuits were originally designed for completely different purposes and had no connection with brain activity. It is a way to measure the eigenvalues, eigenvectors and statistical means of various operators, belonging to the system which are being modeled by electrical means. We briefly discuss below the scheme for handling those things.

Let the wave equation be divided by  $i\omega_c$  where  $\omega_c = \sqrt{\omega} = (E/\hbar)^{\frac{1}{2}}$  and multiplied by  $\Delta x$  we get

$$-\frac{1}{\omega_c} \frac{\hbar^2}{2m} \frac{1}{\Delta x} \frac{\partial^2 \psi}{\partial x^2} \Delta x^2 + \left( \frac{V \Delta x}{i\omega_c} + \hbar i\omega_c \right) \psi = 0 \quad (11)$$

We should like to note some salient points here.

- The Kinetic energy operator  $T$  is represented by a set of inductors in series whose inductance is given by  $L_1 = \frac{2m}{\hbar^2}\Delta x$ .
- The potential energy operator  $V$  is represented by a set of unequal coils in parallel whose inductance is  $L_2 = 1/V\Delta x$ .
- The total energy operator  $-E$  is represented by a set of equal capacitors whose capacitance is  $\hbar\Delta x$ .
- The operand  $\psi$  is represented by voltages and the result of the operation  $\alpha\psi$  where  $\alpha$  is any operator, is represented by currents.

This model can also be extended to nonorthogonal coordinates and in general on arbitrary manifolds. Utilizing the circuits, tests were carried out on an ac network analyzer. The results are worth mentioning. The tests were done in 1-dimensional circuits. or example measurements were made for a particular case of the rectangular potential well and analyzed which had good agreement with the experimental results [28].

For the sake of completeness, we should like to mention here that from the preceding model, we can develop a prescription for developing a electric circuit equivalent for the Schrödinger equation (SE). The SE has some analogies with the heat conduction equation

$$\frac{d\psi}{dt} = \frac{1}{\hbar} \left( \frac{\hbar^2}{2m} \nabla^2 + V \right) \psi \quad (12)$$

Now we make a prescription for the electric circuit as equivalent to the Schrödinger equation as

$$V \Leftrightarrow \psi \quad \frac{1}{r} \Leftrightarrow V\Delta Vol \quad \frac{1}{Rx} \Leftrightarrow \frac{\hbar^2}{2m} \Delta Vol / (\Delta x^2) \quad C \Leftrightarrow i\hbar\Delta Vol \quad (13)$$

The construction relies here on having  $N$  imaginary capacitance and one of the consequence is we will get solutions of the form

$$\psi \sim \exp(ikx) \exp(i\omega t)$$

. Physically this means that we don't have exponential decay with time into thermal equilibrium but we get everlasting solutions which conserve  $|\psi|^2$ . This may sound somewhat unrealistic and there are some ways of circumventing this problem.

## 5 Quantum Mechanics in Ion Channels and the Formulation

Motivated by the quantum mechanical considerations and the circuit equivalence of Schrödinger equation we will now try to formulate an equivalent circuit for the membrane potential in

the ionic channels. We will consider a single ion channel and consider the circuit implementation for it. But there are some subtleties regarding this. Tensor network theory [30] may be realized in the brain and there is possibility of a non trivial geometrical structure inside brain as mentioned by Amari [29], Roy and Kafatos [?]qmic5). Pribram's [31] work also points towards this direction. This implies that there is an underlying geometrical structure inside brain and it may be important at the ionic scales. So we try to develop a formalism for describing that. We start with some simplifying propositions:

- There is an underlying geometry inside brain which is responsible for neuronal activities and the geometry can be described by a metric.
- Quantum mechanics is applicable at the length scales of ionic channels and the phenomena can be described by Schrödinger equation
- The phenomena at those length scales is stochastic.

With these propositions we can now think of a formalism for various set of events inside the brain. It should be mentioned here that ultimately we would like to connect our formalism to the HH formalism, which has been successful in describing the membrane gating and dynamical phenomena involving channels [32].

So we start by writing a SE equation on a curved manifold. The equation can be identified with a Heat Kernel equation.

$$i\hbar \frac{\partial \psi}{\partial t} = \frac{1}{\sqrt{g}} \partial_{\mu} (\sqrt{g} \partial_{\mu} \psi) + V \psi \quad (14)$$

The equation above, for arbitrary metric, is in general, nonlinear and in accordance with our third proposition we claim that the processes are stochastic in nature and the analysis of section 3 tells us that the dynamics will be governed by Riccati like equation [10] with a correction in the potential term as

$$i\hbar \frac{\partial \psi}{\partial t} = \frac{\hbar^2}{2m} \nabla^2 \psi + (V + \frac{\chi(q) \hbar^2 \sqrt{N} \vartheta}{6}) \psi \quad (15)$$

$\vartheta$  is the curvature scalar, associated with the metric, which gets incorporated into the potential term. It is important to note that the correction term differs from that of equation [10] in a coordinate dependent factor. We will show that this factor is crucial in developing a quantum equivalent of a circuit. The mass is absorbed in the coordinate dependent term. The  $\chi$  in some sense acts as a space modulation factor which governs both the noncommutative aspects and the fluctuations from the metric. It should be mentioned here that this equation describes the dynamics for  $N$  channels and we have made a conjecture by including the number of channels, with a hope to get the classical picture of the HH equation in global limit.

The Schrödinger equation along with the correction of the quantum term is a good starting point in our case to develop a circuit equivalent. Actually the problem in this case to extend the previous construction for the equivalence of SE to electrical circuit is



dictated by the presence of the metric. First of all, the metric is a dynamical variable which governs the behavior of space time. So, we cannot just implement it as some electrical component, since such a component should have the ability to shape the global structure of the full circuit. At the moment, we do not know of any such component. We have seen that in periodically driven circuits, we can scale the capacitance or say the inductance as  $L \sim \gamma g(t)$  which may capture, in some sense, the global dynamics, but it will not catch the full glimpse of the dynamical behavior. The curvature gets into the potential term and thereby fluctuations in the metric will induce different potentials and hence only periodic variations may not do [33, 34]. It is a widely held that fundamental processes of nature may be explained by probabilistic metric and the probabilistic features can be modeled into uncertainties or fluctuations from a physical point of view. If we introduce the fluctuations in the metric as

$$g_{ij}(x, h) = g_{ij}(x) + \alpha_{ij}(h)$$

the fluctuation of the metric generates a random potential  $V$ , a random coefficient  $S$  which depends on the fluctuations. In the quantum case we will do indeed get dissipation which depends on the fluctuation. The Schrödinger equation turns to be

$$\frac{\hbar^2}{2} \frac{\partial^2 \phi}{\partial r^2} + V\phi = S \frac{\partial \phi}{\partial t} \quad (16)$$

To make connections with brain activities and neuronal circuits we try to develop circuits corresponding to quantum mechanics, the circuit will do contain some flavor of the noncommutative aspects.

We know that brain phenomena is considered as dissipative. In such kind of theories, one considers such one particle dissipation in quantum theory. So, we try to extend that formalism in our case with the corrected potential along with a source term. Then we consider the following Hamiltonian as:

$$H = -e^{-Rt/L} \frac{\hbar^2}{2e^2 L} p^2 + e^{Rt/L} \left( \frac{1}{2C} q^2 + \varepsilon q + \frac{\chi(q) \vartheta \hbar^2 \sqrt{N}}{6} \right) \quad (17)$$

Here  $q$  is state variable,  $p$  the conjugate which goes uplifted to the charge operator when we deal with quantum mechanics (QM). Using the Heisenberg equation of motion, the equation for the state variable is given by

$$L \frac{d^2 q}{dt^2} = \frac{1}{2e^2} \left( \left\{ \frac{1}{2C} q^2 + \varepsilon q + \frac{\chi(q) \vartheta \hbar^2 \sqrt{N}}{6}, [p^2, q] \right\} \right) - R\dot{q} \quad (18)$$

So, evaluation of the simple commutator gives us the equation for the corresponding quantum circuit as

$$L\ddot{q} + R\dot{q} + \frac{q}{C} = \varepsilon + \frac{\alpha \hbar^2 \sqrt{N}}{6} \vartheta \dot{q} \int dt \chi'(q) \quad (19)$$

The last term in the above equation is most striking. It shows that the above equation clearly shows that the inductance gets corrected, by a quantum term. In this

way, ultimately, at the level of circuit equivalence, we will be getting a renormalized inductance. It gives the equation a status of an integral equation and would be interesting to find out the conditions under which it will reduce to a differential equation. In that case, the capacitance gets renormalized.

It is very important so as to make some measurements to find out these extra factors. There is an extra parameter in the theory which needs to be fine tuned to get the desired effects. The above equation can also be transformed into a Langevin like form and get a measure for the Probability functional, which is very non trivial due to the presence of the curvature term and may hint at some statistical manifold like character. This is not quite surprising as we mentioned at the beginning of the section that it may arise due to the intrinsic stochasticity of the neuronal activities. The above observations have some interesting consequences with respect to Nonlinear Schrodinger Equation. Some of the results is worth mentioning . If we had included in the Schrödinger equation a damping factor in the form of a bounded negative operator and a quasi periodic force, the solutions turn out to be even and periodic. The analysis in such case, give rise to the existence of invariant manifolds in the phase space of the equation. The infinitely many eigenvalues in the integrable limit turn into complex eigenvalues with negative real parts. The manifolds exhibit a dynamical behavior and the geometry resembles those of certain homolonic orbits in finite dimensional Ordinary Differential Equation (ODE [35]).

## 6 Discussions

The striking aspect of our result is that in the most general case, for scales in which QM is applicable, we have found out a generalized HH equation with the conductances  $G_A$  being corrected with the renormalized in equation [2] by

$$G_A + \left(\frac{\alpha\hbar^2\sqrt{N}}{6}\partial\dot{q}\int dt\chi'(q)\right)^{-1}$$

It is necessary to study following two issues. Firstly, to see under what limit does this modified equation i.e., generalized HH equation turns to ordinary equation with no renormalization. Then, one needs to do the experiments to see whether the conductances indeed do get corrected. If it is so then we could measure such term for single ion channels. We also believe that one of the mechanisms by which we may get ordinary HH theory with no renormalization (i.e quantum mechanics is unimportant) is when there are many channels and quantum mechanics is getting subdued in the large  $N$  limit. Anyway, there is a subtle point here. In confirmation of the relevant observation for the stochasticity of HH equation in the Langevin description, we see that in the classical limit, we may get stochasticity for a critical large value of the number of channels. It is really important to design experiments to measure critical parameters as appeared in the above equation. Such experiments will be very conclusive for the correctness of the model and also give

a direct evidence for the applicability of QM in ion channels. It is also to measure the effective conductance. At this stage, we still do not know how we can model such mechanisms, but experimental results on single ion channel may surely shed some light in understanding these aspects [36, 37].

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